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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,356	11/21/2000	Shimpei Ushio	USHIO-2	8174

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/716,356	USHIO ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 18-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2 and 4-9* is/are allowed.

6)☒ Claim(s) *18-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 1, 2, 4-9, and 18-52 are pending and under consideration in this application. Claims 1,2, and 4-9 were indicated to be allowable, and claims 18-52 were rejected, in the prior action mailed on February 17, 2004. In the Response filed on August 5, 2004, the Applicant amended claims 18, 19, and 21.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. **(Prior Rejection- Maintained)** Claims 18-52 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been amended to read on a pharmaceutical composition comprising SEQ ID NO: 6, or a fragment or homologue thereof, wherein the composition is administered in combination with or without a biologically active compound. The Applicant has amended the and argues that the amendment makes "clear that the pharmaceutical composition is administered to a subject after being processed in combination with or without a biologically active compound." However, claims are not drawn to a method of administration, but to a composition. Thus, the mode of administration appears to be an intended use for the composition, and not a structural limitation. It is therefore still unclear if the claim is

requiring the presence of the additional (to the polypeptide of SEQ ID NO: 6) biologically active compound in the claimed composition. If the Applicant intends that the potential inclusion of this compound be a limitation on the claimed composition, it is suggested that the paragraph of part (ii) of the claim be amended to read as follows:

> (ii) a pharmaceutically acceptable carrier, and
>
> (iii) may optionally comprise one or more compounds selected from the group consisting of an adjuvant, excipient, diluent, stabilizer, and a second biologically active compound, said pharmaceutical composition being administered to a subject.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **(Prior Rejection- Withdrawn)** Claims 18, 20-52 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. These claims read, in relevant part, on pharmaceutical compositions comprising fragments of the interferon-γ inducing protein of SEQ ID NO: 6. It is noted that, unlike in claims 1 and 19, claim 18 and its dependant claims did not require that the fragments of the polypeptide have interferon-γ inducing activity. In view of the amendment of the claims such that the fragments, as well as the protein of SEQ ID NO: 6, are required to have this activity, the rejection is withdrawn.

6. **(Prior Rejection- Withdrawn)** Claim 21 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This claim was

amended to read on read on the pharmaceutical compositions of claim 18 comprising a biologically active agent selected from a specific group of compounds to a biologically active agent selected from the group consisting of antitumor agents, antiviral agents, antiseptics, immunotherapeutic agents, platelet-increasing agents, and leukocyte-increasing agents. In view of the amendment to the claim such that it no longer purports to identify the genus of potential biologically active compounds, but rather describes the composition comprising the interferon-γ producing polypeptide, the rejection is withdrawn.

7. **(Prior Rejection- Maintained)** Claims 18, 20, and 21-52 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising SEQ ID NO: 6, or for derivatives thereof varying from SEQ ID NO: 6 by one amino acid residue, does not reasonably provide enablement for a composition comprising any homologue of the sequence that maintains the biological activities and other characteristics required by claim 18.

The Applicant traverses the rejection on three grounds. First, the Applicant argues that the specification and the art provide teachings relating to the state of the art. The second argument is that the cancellation of the homologue language from the claims would result in the ability of those in the art to easily obtain such homologues and thereby practice substantially the same invention without fear of infringing the Applicant's patent. Finally, the Applicant argues that the art demonstrates that homologues of SEQ ID NO: 6 would be effective for the induction of IL-18 production in human cells.

The Applicant's first argument in traverse is that the specification enables those in the art to easily identify homologues to the claimed invention. However, the section of the application referred to provide very little guidance as to the full scope of homologues included by the claims. In particular, page 215 provides only generic teachings relating to the structure of the claimed polypeptides, and neither provides any teachings relating to correlations between any particular structure within SEQ ID NO: 6 that are associated with the indicated characteristics, or provide any guidance as to where operative homologues may be found. Page 28 provides equally broad teachings without specific examples, stating only that homologues may comprise sequences obtained by replacing one or more amino acids with another. These teachings do not provide any examples or other evidence to demonstrate that the Applicant has enabled those in the art to easily identify homologues of the IL-18 described in claim 1, part (a). In view of the unpredictability in the art and the breadth of the claims as described in the prior action, these general teachings are not sufficient to overcome the rejection. This argument is therefore not found persuasive.

The addition of new subpart (6) to claim 18 is noted. However, it is not clear what relevance this amendment has to the issue of the scope of enablement of the claims. The newly added limitation merely requires that the polypeptide of SEQ ID NO: 6 and its homologues are detectable using antibodies specific for those polypeptides. It is an inherent property to a protein that it would be detectable by an antibody specific for that protein. The ability of such antibodies to detect the proteins does not add any further guidance as to the structures of the claimed homologues, or the association of those structures to the requisite biological functions required

by the claims. Thus, the addition of this limitation is not found persuasive in overcoming the rejection.

The second argument in traversal, that the deletion of the homologue language would permit others to use homologues without infringing the Applicant's patent, is not found persuasive. This would be a natural consequence of the deletion of the rejected language, and is not evidence that the Applicant has provided an enabling disclosure. Applicant's reference to the Hwang reference, which discloses a homologue that should, according to the Applicant, fall within the scope of the claims is noted. However, even if it is accepted for the sake of argument that the homologue disclosed therein is enabled by the current application, this is not evidence that the Applicant has enabled the use of any homologue. The scope of homologues that fall within the scope of the present claims are not limited by any means other than by function. There is no percent identity or other structural means of identifying such homologues, nor any guidance as to what residues or structures within the protein of SEQ ID NO: 6 are necessary for the indicated functions, and are required in the claimed homologues. In view of this lack of guidance, the Applicant is not enabled for the full scope of the claimed invention. The existence of later published art teaching potential homologues, with no other relationship to the question of enablement, does not demonstrate to the contrary. This argument then is also found unpersuasive.

Finally, the Applicant asserts that the art is contrary to the Examiner's assertion that the has been no showing that a murine IL-18 would be capable of inducing INF-γ production in human cells. However, the reference cited by the Applicant is not found persuasive. The Examiner agrees that the reference does, as the Applicant states, show "that murine IL-18 binds

to cells derived from human and acts on cells to induce interferon-gamma production." However, the term "derived from" should be considered. The art teaches that the human cells had to be modified to express murine IL-18 receptor before it would respond to the murine IL-18. Thus, the reference does not demonstrate that any human cells would be responsive to any IL-18 homologue. Rather, the reference demonstrates that human cells do not, without modification, respond to such homologues. Because the reference indicates that such specific modification is required for homologues to work, and because the claims are silent as to the requirement for such modification, the Applicant's arguments are not found persuasive. The rejection is therefore maintained.

8. **(Prior Rejection- Maintained)** Claims 18, 20, and 21-52 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims were rejected because the Application does not provide adequate support for claims to the genus of all homologues to the interferon-gamma inducing factor (IGIF) of SEQ ID NO: 6. The Applicant traverses the rejection on the grounds that the claims set forth a set of physiochemical properties, and that these properties correlation to the required function, and that the application discloses a number of species within the claimed genus. These arguments are not found persuasive.

The Examiner agrees with the Applicant's characterization of the claims with reference to the scope of homologues claimed (those with the properties of sections (2)-(6) of the claim).

However, the Examiner does not agree that the Applicant has either established that these properties correlate with the required function (in part (4) of the claim) or that there are multiple examples of species of homologues such that the genus of homologues is adequately represented.

As was indicated in the prior action, with the exception of the protein of SEQ ID NO: 6 itself, the application has not provided any examples of the polypeptides falling within the scope of the claimed invention. While the Applicant has asserted that such examples exist, it is noted that no specific reference to such examples has been provided in the Response.

In addition to the lack of examples, there is also no structural or other non-functional means of identifying the members of the claimed genus. As was indicated by the Applicant on page 15 of the Response, the physiochemical characteristics listed in claim 18 represent the functional aspects of the indicated genus. The Applicant also asserts that the amino acid sequence of SEQ ID NO: 6 represents the structural component of the claimed genus. However, neither the claims nor the specification anywhere require that the homologues have this amino acid sequence, or any portion thereof. Thus, in view of the lack of any structural or other non-functional means of identifying the members of the claimed genus, and the lack of examples of such homologues, the Applicant's assertion of written description support appears to be unfounded. The rejection is therefore maintained.

Conclusion

9. Claims 1, 2, and 4-9 are found allowable.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 9/7/04

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